

10/8/4, 194  
L/COOK 12/7/05

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(FILE 'HOME' ENTERED AT 16:21:50 ON 07 DEC 2005)

FILE 'STNGUIDE' ENTERED AT 16:21:54 ON 07 DEC 2005

FILE 'HOME' ENTERED AT 16:21:59 ON 07 DEC 2005

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT  
16:22:19 ON 07 DEC 2005

L1 61 S (ANTI PAF) AND ASSAY?  
L2 35 S L1 AND PD<1999  
L3 12 S L2 AND HUMAN?

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10/814, 194  
Lyceek 10/7/05

d his

(FILE 'HOME' ENTERED AT 09:53:28 ON 07 DEC 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT  
09:53:55 ON 07 DEC 2005

L1 617 S PAF AND PREGNANCY  
L2 431 S (ANTI PAF)  
L3 0 S L2 AND ABORTION?  
L4 199 DUPLICATE REMOVE L2 (232 DUPLICATES REMOVED)  
L5 149 S L4 AND PD<1999  
L6 7 S L1 AND L2  
L7 5 DUPLICATE REMOVE L6 (2 DUPLICATES REMOVED)

=>

d his

(FILE 'HOME' ENTERED AT 09:53:28 ON 07 DEC 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT  
09:53:55 ON 07 DEC 2005

L1 617 S PAF AND PREGNANCY  
L2 431 S (ANTI PAF)  
L3 0 S L2 AND ABORTION?  
L4 199 DUPLICATE REMOVE L2 (232 DUPLICATES REMOVED)  
L5 149 S L4 AND PD<1999  
L6 7 S L1 AND L2  
L7 5 DUPLICATE REMOVE L6 (2 DUPLICATES REMOVED)

=>

ANSWER 10 OF 149 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN  
AN 1996:227510 BIOSIS  
DN PREV199698783639  
TI Effect of platelet-activating factor (PAF) on preimplantation mouse  
B-6D-2F-1/J embryo formation.  
AU Roudebusch, William E. [Reprint author]; Duralia, David R.; Butler, William  
J.  
CS Div. Reproductive Endocrinol., Dep. Obstetrics Gynecol., Med. Univ. South  
Carolina, Charleston, SC 29425-2233, USA  
SO American Journal of Reproductive Immunology, (1996) Vol. 35, No.  
3, pp. 272-276.  
ISSN: 1046-7408.  
DT Article  
LA English  
ED Entered STN: 8 May 1996  
Last Updated on STN: 8 May 1996  
AB Platelet-activating factor (1-O-alkyl-2-acetyl-sn-glycero-3-phosphocholine;  
PAF) is a potent signaling phospholipid that has been implicated in a  
variety of reproductive processes. Human, rabbit, and mouse  
preimplantation embryos produce and secrete PAF. Anti-  
PAF antibodies interfere with mouse preimplantation development.  
A controversy exists on whether exogenous PAF is beneficial to  
preimplantation embryo development. The study objective was to determine  
the effect of exogenous PAF on embryo formation. One-cell mouse  
B-6D-2F-1/J embryos were collected from PMSG/hCG primed females mated with  
fertile males. Embryos were exposed to PAF (0-10  $\mu$ M) in MEM (0.3% BSA)  
for 15 min, then cultured in MEM (0.3% BSA) in a 5% CO<sub>2</sub> in air, 95%  
relative humidity at 37 degree C atmosphere, for 120 hr to the hatched  
blastocyst stage. PAF (0.1 or 0.01  $\mu$ M) significantly ( $P < 0.05$ )  
improved preimplantation embryo development and formation in vitro. PAF  
at higher doses had no significant effect. Supplementation of culture  
medium with exogenous PAF was beneficial to preimplantation embryo  
development in B-6D-2F-1/J mice.  
CC Cytology - Animal 02506  
Biochemistry studies - Proteins, peptides and amino acids 10064  
Biochemistry studies - Lipids 10066  
Reproductive system - Physiology and biochemistry 16504  
Endocrine - General 17002  
Development and Embryology - Experimental 25504  
IT Major Concepts  
Cell Biology; Development; Endocrine System (Chemical Coordination and  
Homeostasis); Reproductive System (Reproduction)  
IT Miscellaneous Descriptors  
SIGNALING PHOSPHOLIPID  
ORGN Classifier  
Muridae 86375  
Super Taxa  
Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
Muridae  
Taxa Notes  
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,  
Rodents, Vertebrates

ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1989:70050 CAPLUS

DN 110:70050

ED Entered STN: 04 Mar 1989

TI Compositions and methods for fertility control using platelet-activating factor, its analogs and antagonists

IN O'Neill, Christopher

PA Royal North Shore Hospital, Australia

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-685

ICS A61K031-55; A61K031-557; A61K037-64; A61K031-47; A61K031-20;  
A61K031-34; A61K031-565; A61K037-02

CC 2-3 (Mammalian Hormones)

FAN.CNT 1

|    | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|----|---|------|----------|-----------------|----------|
| PI | EP 261798   | A2   | 19880330 | EP 1987-307439  | 19870821 |
|    | EP 261798   | A3   | 19900509 |                 |          |
|    | R: AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|    | AU 8777189  | A1   | 19880225 | AU 1987-77189   | 19860822 |
|    | AU 608530   | B2   | 19910411 |                 |          |
|    | US 4879285  | A    | 19891107 | US 1987-86900   | 19870818 |
|    | DK 8704315  | A    | 19880223 | DK 1987-4315    | 19870819 |
|    | ZA 8706215  | A    | 19880427 | ZA 1987-6215    | 19870821 |
|    | JP 63115819                                       | A2   | 19880520 | JP 1987-209119  | 19870822 |
|    | PRAI AU 1986-7642                                 | A    | 19860822 |                 |          |

CLASS

|  | PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES  |
|--|------------|-------|---|
|  | EP 261798  | ICM   | A61K031-685   |
|  |            | ICS   | A61K031-55; A61K031-557; A61K037-64; A61K031-47;<br>A61K031-20; A61K031-34; A61K031-565; A61K037-02 |
|  | US 4879285 | NCL   | 514/075.000; 514/120.000; 514/841.000; 514/843.000  |

OS MARPAT 110:70050

AB The in vivo or in vitro administration of platelet-activating factor [sn-R2OCH2CH(O2CR1)CH2OP(:O)(O-)OCH2CH2N+R33 (I; R1 = R3 = Me; R2 = C16 or C18 alkyl)] (PAF) or PAF analogs (I; R1 = C1-6 alkyl;

R2 = C10-24 alkyl; R3 = C1-3 alkyl) enhances the viability of fertilized embryos and improves rates of implantation in the uterus. Conversely, reduction of PAF concentration by in vivo administration of PAF antagonists such as iloprost or anti-PAF antibodies

has a contraceptive effect, particularly when used in conjunction with a postcoital contraceptive such as estrogen or a prostaglandin.

Ovulation-synchronized mice were mated and iloprost (PAF antagonist) was administered at 1.0 or 2.0 µg/30 g body weight i.p. 6 times on days 1-4 of pregnancy. The implantation rate was decreased from about 75% in controls to 40-50% by this treatment. In contrast, when 2-cell embryos collected from superovulated mated mice were cultured to the blastocyst stage in human tubal fluid medium containing bovine serum albumin and PAF (0.1 µg/mL) and transferred to pseudopregnant females on day 3 of pseudopregnancy, the implantation rate was increased from 34.3 (control) to 58.6%.

ST fertility control platelet activating factor; contraceptive iloprost; embryo implantation platelet activating factor

IT Fertility

(blood platelet-activating factor and antagonists effect on)

IT Contraceptives

(blood platelet-activating factor antagonists)

IT Uterus

(embryo implantation in, blood platelet-activating factor and antagonists effect on)

IT    Embryo  
      (implantation of, blood platelet-activating factor and antagonists  
      effect on)

IT    Corpus luteum  
      (progesterone secretion by, blood platelet-activating factor effect on)

IT    Antibodies  
      RL: BIOL (Biological study)  
          (to blood platelet-activating factor, as contraceptives)

IT    15291-77-7, BN 52021 28981-97-7, Alprazolam 78919-13-8, Iloprost  
      95851-37-9, Kadsurenone 99103-35-2, L 652731 104786-62-1, SRI 63441  
      109516-82-7, SRI 63675 118817-52-0, SRI 64412 118817-53-1, SRI 64557  
      RL: BIOL (Biological study)  
          (as contraceptive)

IT    65154-06-5, Blood platelet-activating factor  
      RL: BIOL (Biological study)  
          (fertility control with)

IT    57-83-0, Progesterone, biological studies  
      RL: BIOL (Biological study)  
          (secretion of, by corpus luteum, blood platelet-activating factor  
          effect on)

IT     **Embryo**  
          (implantation of, blood platelet-activating factor and antagonists  
          effect on)

IT     **Corpus luteum**  
          (progesterone secretion by, blood platelet-activating factor effect on)

IT     **Antibodies**  
          RL: BIOL (Biological study)  
          (to blood platelet-activating factor, as contraceptives)

IT     15291-77-7, BN 52021 28981-97-7, Alprazolam 78919-13-8, Iloprost  
95851-37-9, Kadsurenone 99103-35-2, L 652731 104786-62-1, SRI 63441  
109516-82-7, SRI 63675 118817-52-0, SRI 64412 118817-53-1, SRI 64557  
RL: BIOL (Biological study)  
          (as contraceptive)

IT     65154-06-5, Blood platelet-activating factor  
          RL: BIOL (Biological study)  
          (fertility control with)

IT     57-83-0, Progesterone, biological studies  
          RL: BIOL (Biological study)  
          (secretion of, by corpus luteum, blood platelet-activating factor  
          effect on)

ANSWER 4 OF 5 MEDLINE on STN

AN 95329913 MEDLINE

DN PubMed ID: 7606155

TI Anti-platelet activating factor (PAF) antibody inhibits CFW mouse preimplantation embryo development.

AU Roudebush W E; Mathur S; Butler W J

CS Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston 29425-2233, USA.

SO Journal of assisted reproduction and genetics, (1994 Sep) 11 (8) 414-8.  
Journal code: 9206495. ISSN: 1058-0468.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199508

ED Entered STN: 19950828

Last Updated on STN: 19950828

Entered Medline: 19950814

AB OBJECTIVE: Our purpose was to investigate the effect of anti-PAF antibodies on CFW mouse embryo development in vitro. DESIGN: We studied the in vitro development of CFW mouse one-cell-stage embryos cultured in MEM supplemented with anti-PAF, anti-IgG, or MEM alone to the hatched blastocyst stage. RESULTS: Mouse embryos cultured with anti-PAF (1:5 dilution; 61%) significantly decreased embryo development compared to controls (MEM alone; 93%), whereas embryos cultured in anti-mouse IgG-supplemented MEM (1:10 dilution; 93%) had no effect. CONCLUSIONS: The results provide additional evidence that PAF is produced and secreted by cleavage-stage embryos and is required during the preimplantation period.

CT Check Tags: Female; Male

Animals

\*Antibodies: IM, immunology

\*Antibodies: PD, pharmacology

Blastocyst: DE, drug effects

Blastocyst: IM, immunology

Blastocyst: PH, physiology

Cells, Cultured

\*Embryonic Development: IM, immunology

\*Embryonic and Fetal Development: IM, immunology

Horses

Humans

Immunoglobulin G: IM, immunology

Mice

Mice, Inbred Strains

\*Platelet Activating Factor: IM, immunology

Platelet Activating Factor: ME, metabolism

Platelet Activating Factor: PD, pharmacology

Pregnancy

Sheep

CN 0 (Antibodies); 0 (Immunoglobulin G); 0 (Platelet Activating Factor)

ANSWER 4 OF 5 MEDLINE on STN

AN 95329913 MEDLINE

DN PubMed ID: 7606155

TI Anti-platelet activating factor (PAF) antibody inhibits CFW mouse preimplantation embryo development.

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Blastocyst: PH, physiology

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\*Embryonic and Fetal Development: IM, immunology

Horses

Humans

Immunoglobulin G: IM, immunology

Mice

Mice, Inbred Strains

\*Platelet Activating Factor: IM, immunology

Platelet Activating Factor: ME, metabolism

Platelet Activating Factor: PD, pharmacology

Pregnancy

Sheep

CN 0 (Antibodies); 0 (Immunoglobulin G); 0 (Platelet Activating Factor)

DUPLICATE 1

AN 2001:370034 BIOSIS

DN PREV200100370034

TI Fluorometric detection of platelet activating factor receptor in cultured oviductal epithelial and stromal cells and endometrial stromal cells from bovine at different stages of the oestrous cycle and early pregnancy.

AU Tiemann, U. [Reprint author]; Viergutz, T.; Jonas, L.; Wollenhaupt, K.; Poehland, R.; Kanitz, W.

CS Unit of Reproductive Biology, Research Institute for the Biology of Farm Animals, 18196, Dummerstorf, Germany  
tiemann@fhn-dummerstorf.de

SO Domestic Animal Endocrinology, (April, 2001) Vol. 20, No. 3, pp. 149-164. print.

CODEN: DANEEE. ISSN: 0739-7240.

DT Article

LA English

ED Entered STN: 8 Aug 2001

Last Updated on STN: 19 Feb 2002

AB During the oestrous cycle and early pregnancy, the oviduct and uterus undergo a variety of morphological and physiological modifications in which the platelet activating factor receptor (PAF-R) plays an important role. PAF-R levels were quantified in bovine oviductal epithelial and stromal cells and endometrial stromal cells at days 2 to 4, 12, and 20 of the estrous cycle and during early pregnancy. Cells were grown in vitro and their intracellular PAF-R concentration was measured by flow cytometry using a polyclonal anti-PAF-R antibody system. A significant increase ( $P<0.05$ ) in the portion of PAF-R-positive oviductal epithelial and stromal cells was detected in both non-pregnant and pregnant cattle on days 2 to 4 in comparison to day 12 and 20. In endometrial stromal cells derived from day 20 pregnant bovine, a significant increase ( $P<0.05$ ) in PAF-R staining was observed in comparison to the day 20 non-pregnant and days 2 to 4 or 12 pregnant and non-pregnant animals. The PAF-R was detected in oviductal cells by using immunoblotting and immuno-gold postembedding method. Positive binding of the anti-PAF-R antibody was found on the cell membrane and in the cytoplasm. We concluded that the increased PAF-R concentration measured in cultured oviductal epithelial and stromal cells of cyclic and pregnant heifers on days 2 to 4 was hormonally regulated. The increased PAF-R in endometrial stromal cells on day 20 of pregnant heifers was a pregnancy-specific effect and may mediate a local increase in endometrial vascular permeability known to precede the implantation.

CC Cytology - Animal 02506

Biochemistry studies - General 10060

Reproductive system - Physiology and biochemistry 16504

Animal production - General and methods 26502

Animal production - Breeds and breeding 26506

Immunology - General and methods 34502

IT Major Concepts

Animal Husbandry (Agriculture); Biochemistry and Molecular Biophysics; Reproductive System (Reproduction)

IT Parts, Structures, &amp; Systems of Organisms

cell membrane; cytoplasm; endometrial stromal cells: reproductive system, cultured; oviduct: reproductive system; oviductal epithelial cell: reproductive system, cultured; oviductal stromal cells: reproductive system, cultured; uterus: reproductive system

IT Chemicals &amp; Biochemicals

anti-platelet activating factor receptor [anti-PAF-R]; antibody; platelet activating factor receptor [PAF-R]

IT Methods &amp; Equipment

flow cytometry: cytophotometry: CB, measurement method; fluorometry:

DUPLICATE 1

AN 2001:370034 BIOSIS

DN PREV200100370034

TI Fluorometric detection of platelet activating factor receptor in cultured oviductal epithelial and stromal cells and endometrial stromal cells from bovine at different stages of the oestrous cycle and early pregnancy.

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CS Unit of Reproductive Biology, Research Institute for the Biology of Farm Animals, 18196, Dummerstorf, Germany  
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CC Cytology - Animal 02506

Biochemistry studies - General 10060

Reproductive system - Physiology and biochemistry 16504

Animal production - General and methods 26502

Animal production - Breeds and breeding 26506

Immunology - General and methods 34502

IT - Major Concepts

Animal Husbandry (Agriculture); Biochemistry and Molecular Biophysics; Reproductive System (Reproduction)

IT Parts, Structures, &amp; Systems of Organisms

cell membrane; cytoplasm; endometrial stromal cells: reproductive system, cultured; oviduct: reproductive system; oviductal epithelial cell: reproductive system, cultured; oviductal stromal cells: reproductive system, cultured; uterus: reproductive system

IT Chemicals &amp; Biochemicals

anti-platelet activating factor receptor [anti-PAF-R]; antibody; platelet activating factor receptor [PAF-R]

IT Methods &amp; Equipment

flow cytometry: cytophotometry: CB, measurement method; fluorometry:

detection method, photometry: CB; immuno-gold postembedding method:  
detection method; immunoblotting: detection method

IT Miscellaneous Descriptors

estrous cycle stages; pregnancy

ORGN Classifier

Bovidae 85715

Super Taxa

Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

bovine: female, heifer

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,  
Nonhuman Mammals, Vertebrates

detection method, photometry: CB; immuno-gold postembedding method:  
detection method; immunoblotting: detection method

IT Miscellaneous Descriptors

estrous cycle stages; pregnancy

ORGN Classifier

Bovidae 85715

Super Taxa

Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

bovine: female, heifer

Taxa Notes

Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates,  
Nonhuman Mammals, Vertebrates

ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1989:70050 CAPLUS

DN 110:70050

ED Entered STN: 04 Mar 1989

TI Compositions and methods for fertility control using platelet-activating factor, its analogs and antagonists

IN O'Neill, Christopher

PA Royal North Shore Hospital, Australia

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-685

ICS A61K031-55; A61K031-557; A61K037-64; A61K031-47; A61K031-20;  
A61K031-34; A61K031-565; A61K037-02

CC 2-3 (Mammalian Hormones)

FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | EP 261798   | A2   | 19880330 | EP 1987-307439  | 19870821 |
|      | EP 261798   | A3   | 19900509 |                 |          |
|      | R: AT, BE, CH, DE, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
|      | AU 8777189  | A1   | 19880225 | AU 1987-77189   | 19860822 |
|      | AU 608530   | B2   | 19910411 |                 |          |
|      | US 4879285  | A    | 19891107 | US 1987-86900   | 19870818 |
|      | DK 8704315  | A    | 19880223 | DK 1987-4315    | 19870819 |
|      | ZA 8706215  | A    | 19880427 | ZA 1987-6215    | 19870821 |
|      | JP 63115819                                       | A2   | 19880520 | JP 1987-209119  | 19870822 |
| PRAI | AU 1986-7642                                      | A    | 19860822 |                 |          |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES  |
|------------|-------|---|
| EP 261798  | ICM   | A61K031-685   |
|            | ICS   | A61K031-55; A61K031-557; A61K037-64; A61K031-47;<br>A61K031-20; A61K031-34; A61K031-565; A61K037-02 |
| US 4879285 | NCL   | 514/075.000; 514/120.000; 514/841.000; 514/843.000  |

OS MARPAT 110:70050

AB The in vivo or in vitro administration of platelet-activating factor [sn-R2OCH2CH(O2CR1)CH2OP(:O)(O-)OCH2CH2N+R33 (I; R1 = R3 = Me; R2 = C16 or C18 alkyl)] (PAF) or PAF analogs (I; R1 = C1-6 alkyl; R2 = C10-24 alkyl; R3 = C1-3 alkyl) enhances the viability of fertilized embryos and improves rates of implantation in the uterus. Conversely, reduction of PAF concentration by in vivo administration of PAF antagonists such as iloprost or anti-PAF antibodies has a contraceptive effect, particularly when used in conjunction with a postcoital contraceptive such as estrogen or a prostaglandin.

Ovulation-synchronized mice were mated and iloprost (PAF antagonist) was administered at 1.0 or 2.0 µg/30 g body weight i.p. 6 times on days 1-4 of pregnancy. The implantation rate was decreased from about 75% in controls to 40-50% by this treatment. In contrast, when 2-cell embryos collected from superovulated mated mice were cultured to the blastocyst stage in human tubal fluid medium containing bovine serum albumin and PAF (0.1 µg/mL) and transferred to pseudopregnant females on day 3 of pseudopregnancy, the implantation rate was increased from 34.3 (control) to 58.6%.

ST fertility control platelet activating factor; contraceptive iloprost; embryo implantation platelet activating factor

IT Fertility

(blood platelet-activating factor and antagonists effect on)

IT Contraceptives

(blood platelet-activating factor antagonists)

IT Uterus

(embryo implantation in, blood platelet-activating factor and antagonists effect on)

# Reproduction, Fertility and Development

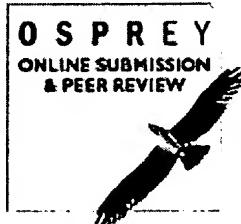
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## Platelet-activating factor-antagonists reduce implantation in mice at low doses only

C O'Neill

### Abstract

The effects of a number of platelet-activating factor (PAF)-antagonists on embryo implantation were investigated. Mice were treated from Day 1 to Day 4 of pregnancy with three defined PAF-antagonists: SRI 63 441, BN 52021, and WEB 2086. Necropsies were performed on Day 8 and the number of implantation sites, the implantation rate (number of implanted embryos compared with the number of corpora lutea) and the proportion of animals pregnant were determined. Each agent caused a reduction in the number of implantation sites at relatively low doses. The dose that had a maximum contragestational effect was 40 micrograms, 10 micrograms and 10 micrograms (per 30 g bodyweight per day) for SRI 63 441, WEB 2086 and BN 52021 respectively. This contragestational effect was completely lost at twice (SRI 63 441), five times (WEB 2086) and ten times (BN 52021) the most effective dose. Treatment with WEB 2086 on the day of implantation (Day 4) by intraperitoneal injection or instillation into the uterus only did not significantly reduce the implantation rate and neither did treatment after implantation (Days 5-8). The results show that the pharmacology of PAF-antagonists in early pregnancy is not simple. An understanding of the actions of these agents in early pregnancy will require a detailed knowledge of their pharmacokinetics, pharmacodynamics and targets of action in early pregnancy.

*Reproduction, Fertility and Development* 7(1) 51 - 57

Full text doi:10.1071/RD9950051

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